

# Supporting Information

## Hyperspectral Mapping for the Detection of SARS-CoV-2 Using Nano-molecular Probes with Yoctomole Sensitivity

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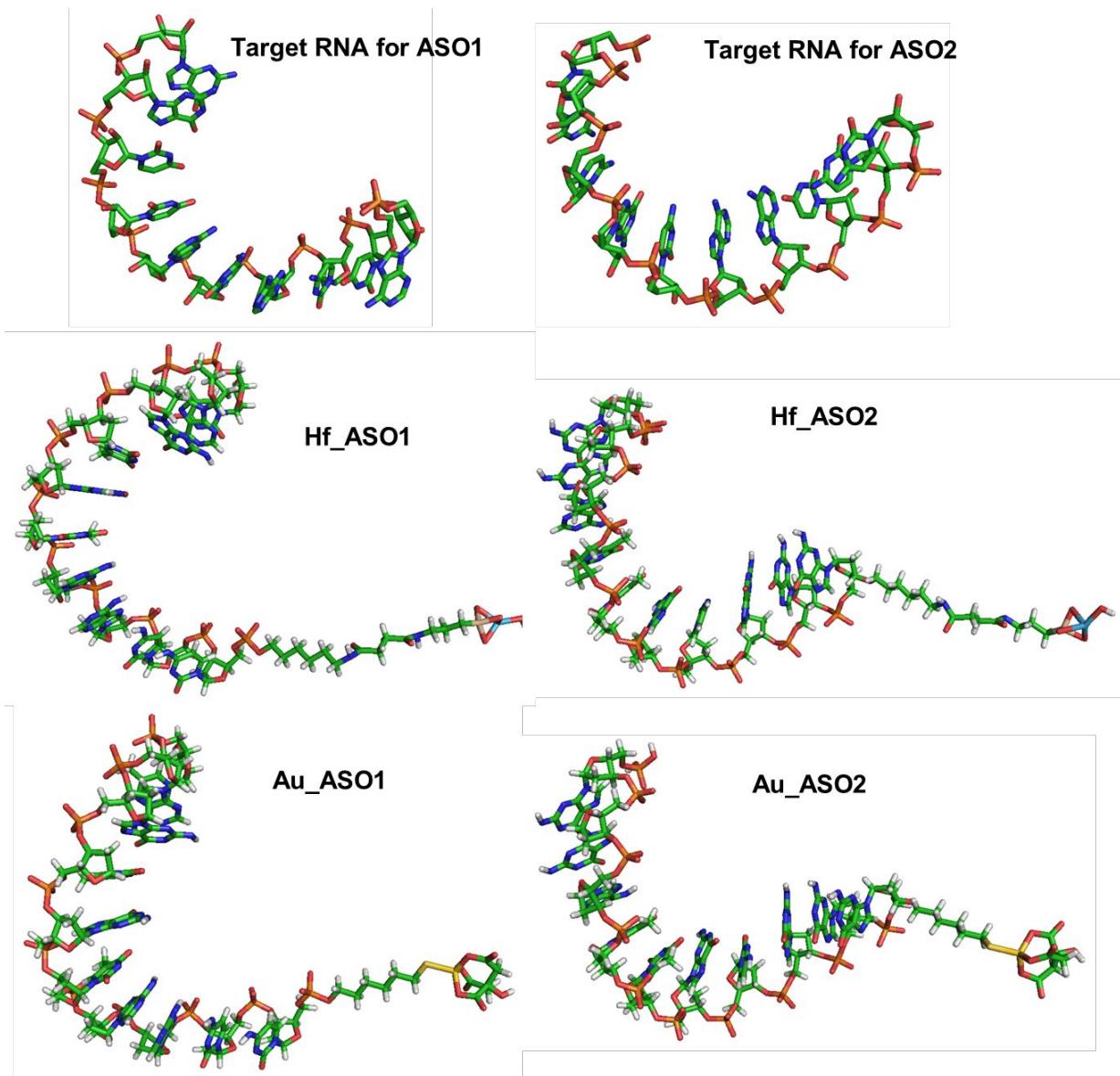
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## Supplementary Data 1

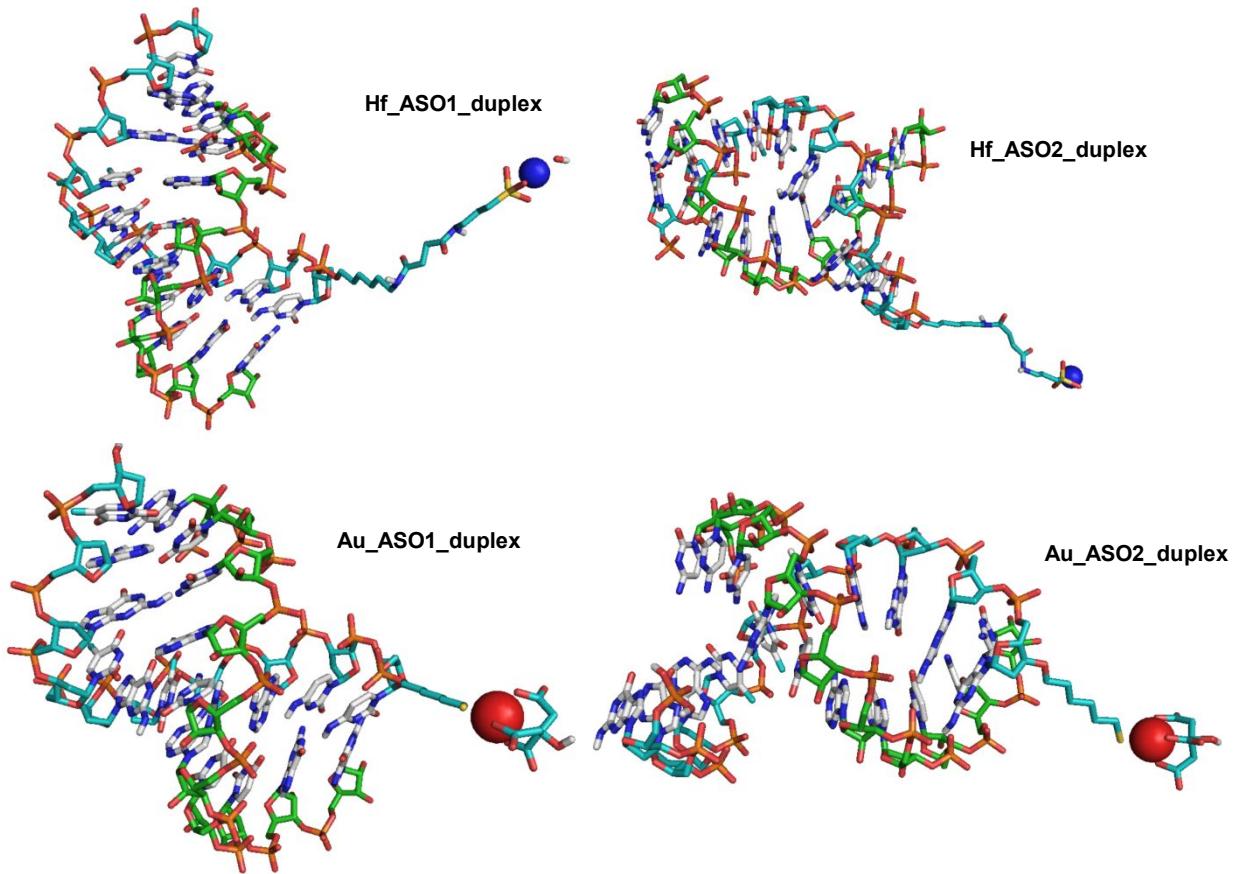
N-gene sequence. Target gene sequence of severe acute respiratory syndrome coronavirus 2 isolate 2019- nCoV/USA-WA1-A12/2020 gene="N" (1260 number of nucleotide bases)  
Accession MT020880 CDS 28274..29533 /product="nucleocapsid phosphoprotein"  
/protein\_id="QHU79201.1"  
/translation="MSDNGPQNQRNAPRITFGGPSDSTGSNQNGERSGARSKQRRPQG  
LPNNTASWFTALTQHKGEDLKPRGQGVINTNSSPDDQIGYYRRATRRIRGGDGKMK  
DLSPRWYFYYLGTGPEAGLPYGANKDGIIVVATEGALNTPKDHIGHTRNPANNAAIVLQL  
PQGTTLPKGFYAEGSRGGSQASSRSSRSRNNSTPGSSRGTSARMAGNGDAALA  
LLLLDRLNQLESKMSGKGQQQQQTVKSAAEASKPRQKRTATKAYNVTQAFGR  
GPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGA  
IKLDDKDPNFKDQVILLNKHIDAYKTFPPTEPKDKKKKADETQALPQRQKKQQTV  
TLLPAADLDDFSKQLQQSMSSADSTQA"

**Table S1.** Sequences considered for theoretical calculations.

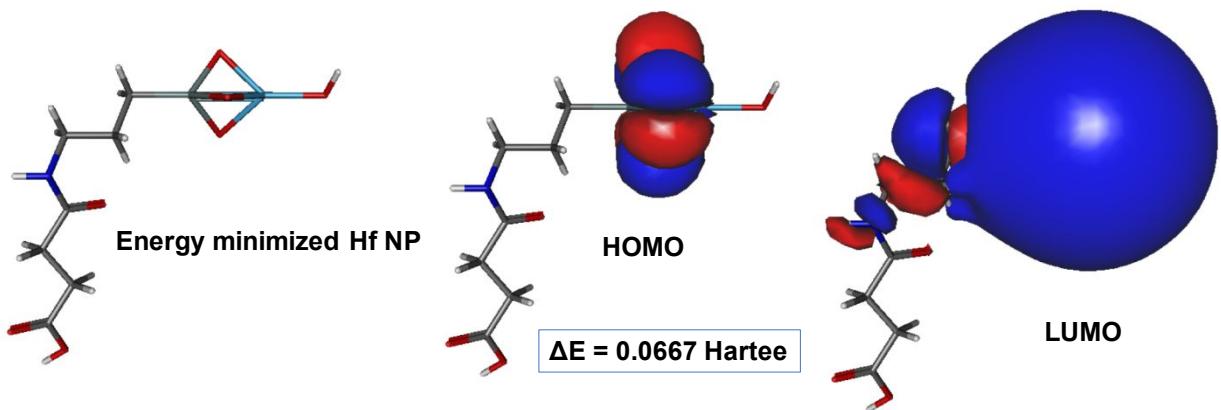
<b>Target RNA sequence</b>	<b>ASO sequences</b>
5'-AUCACAUUUGG-3'	Func-5'-CCAATGTGAT-3' (ASO1)
5'-CCCGCAAUCC-3'	5'-GGATTGCAGGG-3'-Func (ASO2)



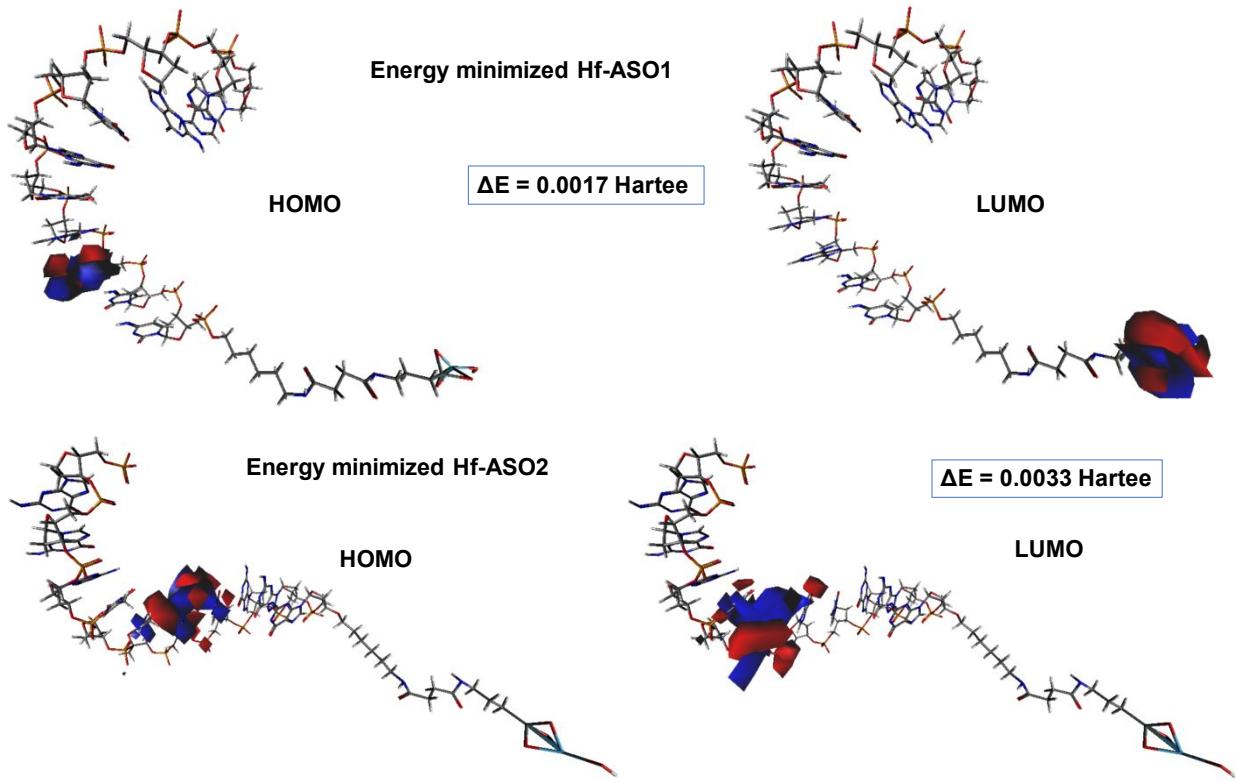
**Fig. S1.** Target RNA and ASO sequence considered for the theoretical calculations are represented in the table. The energy minimized structures of the target RNAs; ASO1 and ASO2 conjugated hafnium and gold nanoparticles are presented below.



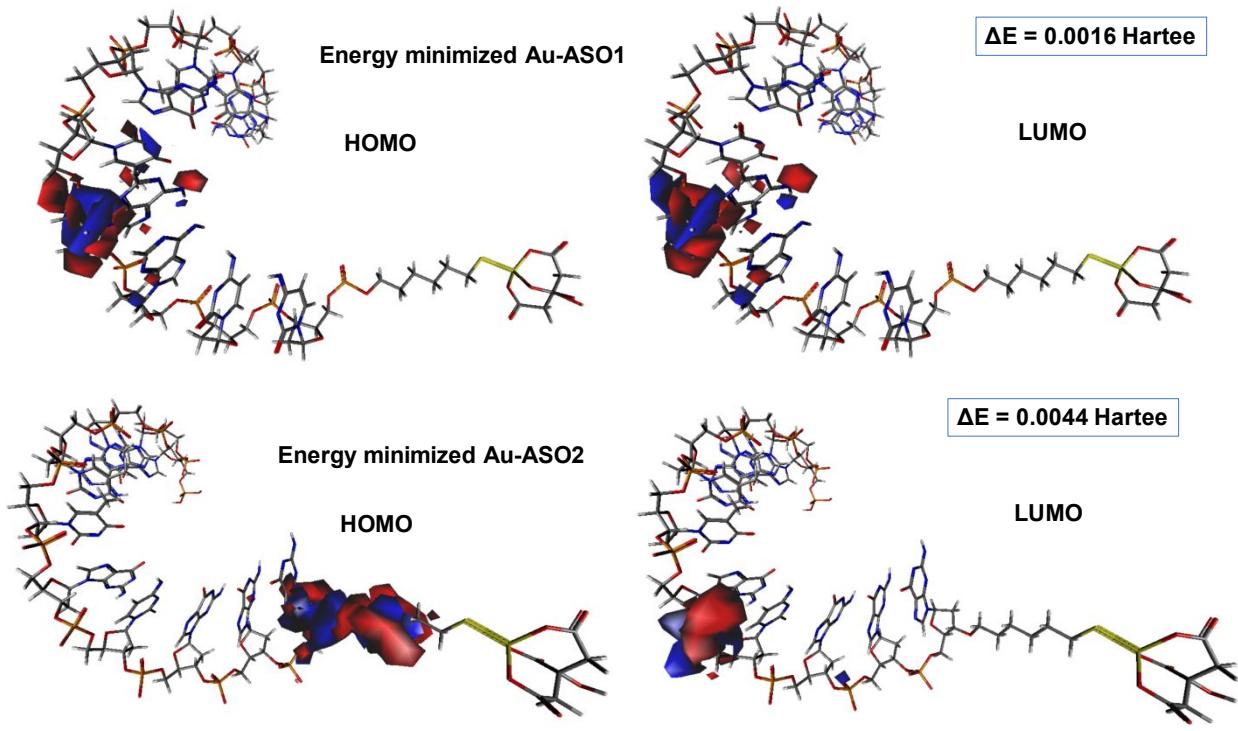
**Fig. S2.** Pictorial representation of the docked geometries between ASO1 and ASO2 conjugated gold or hafnium nanoparticles with their target SARS-CoV-2 RNA sequence.



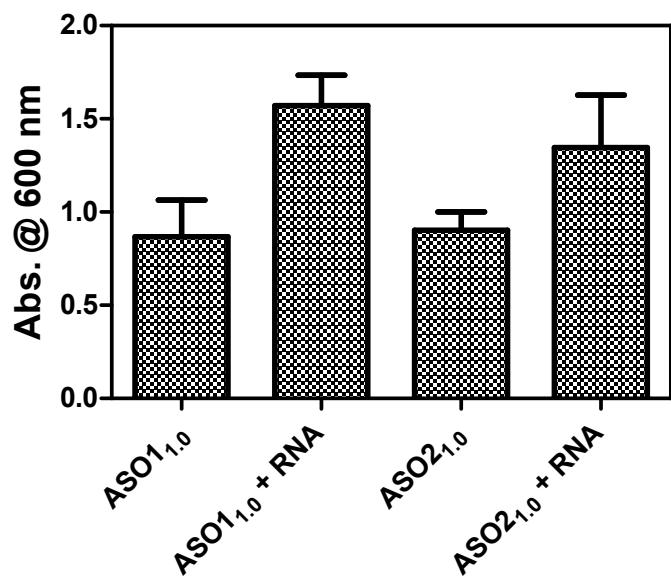
**Fig. S3.** Pictorial diagram of HOMO and LUMO of the energy minimized hafnium nanoparticles.



**Fig. S4.** Pictorial diagram of HOMO and LUMO of the energy minimized ASO1 and ASO2 conjugated hafnium nanoparticles.



**Fig. S5.** Pictorial diagram of HOMO and LUMO of the energy minimized ASO1 and ASO2 conjugated gold nanoparticles.



**Fig. S6.** Change in absorbance at 600 nm of ASO conjugated HfNPs upon addition of SARS-CoV-2 RNA.

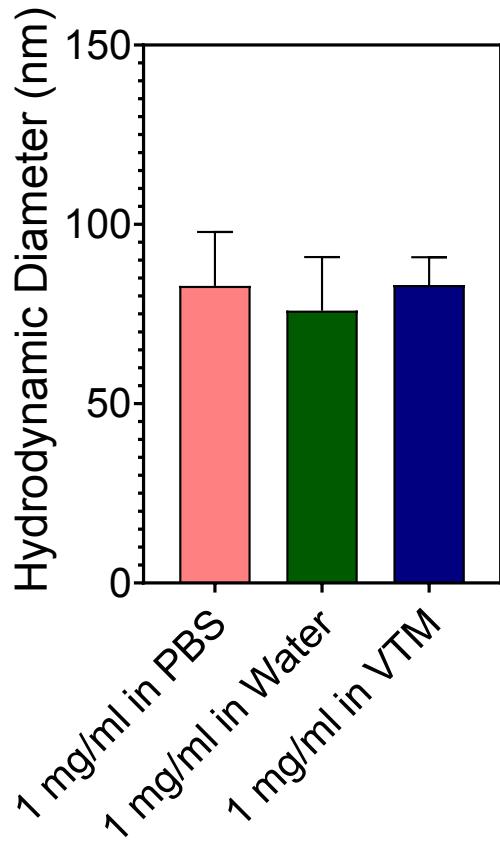


Fig. S7. The effect of the different mediums on the particle size.

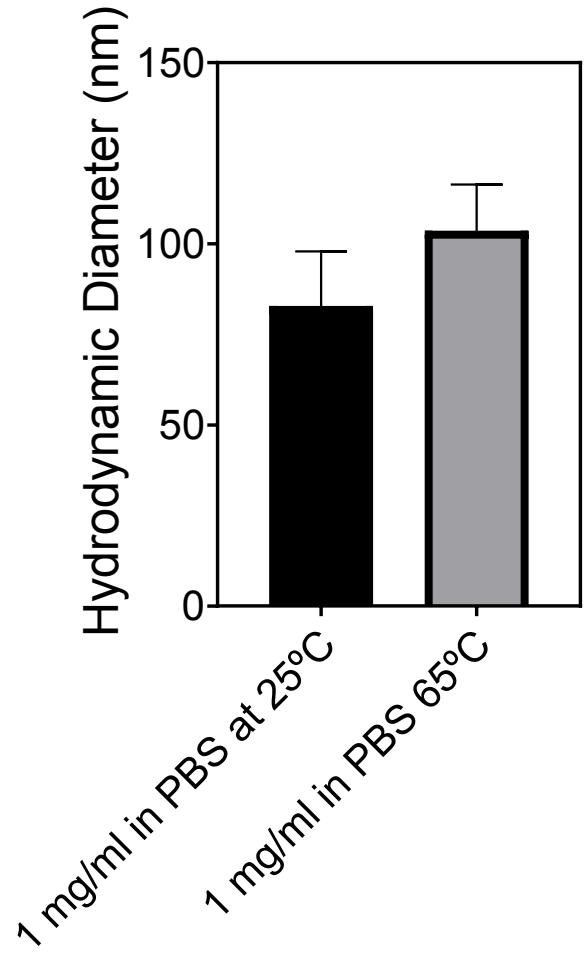
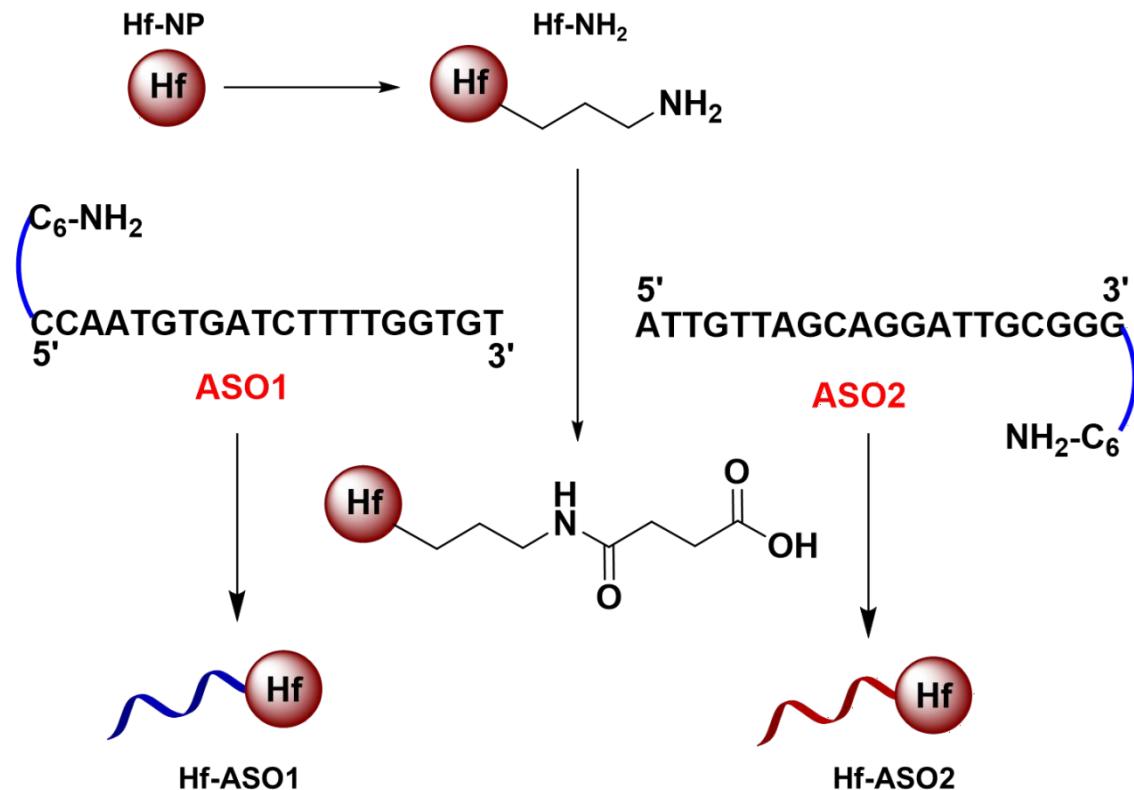
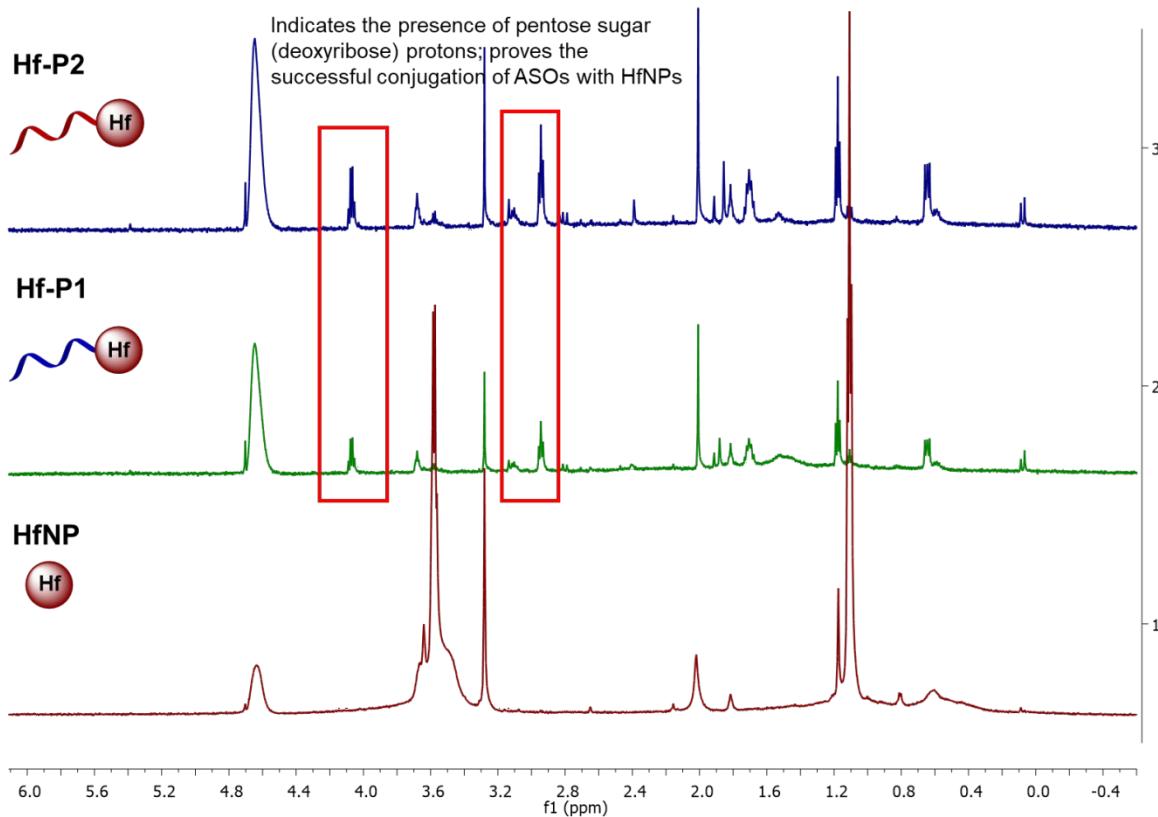


Fig. S8. The effect of temperature on the particle size.



**Fig. S9.** Surface modification of the HfNPs to introduce carboxylic acid moieties on the surface for their functionalization with ssDNA probes.



**Fig. S10.** NMR spectra of HfNP, HfNP conjugated ASO1 (HfNPs-P<sub>1</sub>), and HfNP conjugated ASO1 (HfNPs-P<sub>2</sub>), respectively.

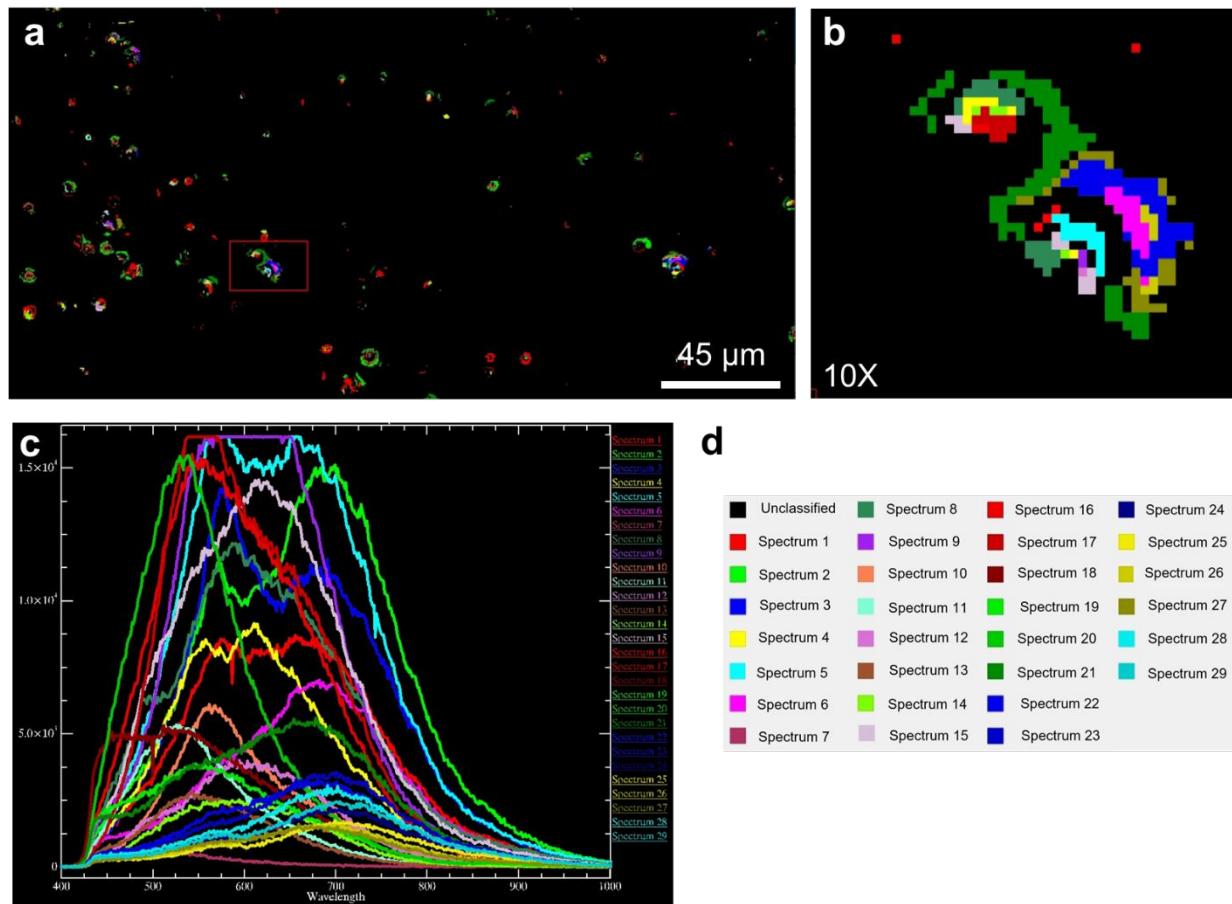


Fig. S11 The hyperspectral mapping of a representative COVID-19 positive clinical sample. a, Hyperspectral mapping of the full field of view of a representative COVID-19 positive sample. b, zoomed in image of a portion of a showing large cluster and the mapping of the hyperspectral signals as represented by the color code. c, the hyperspectral signals associated with the mapping image color coded based on its corresponding color in the mapping image. d, the color code used in establishing the mapping image and its associated spectrum name.

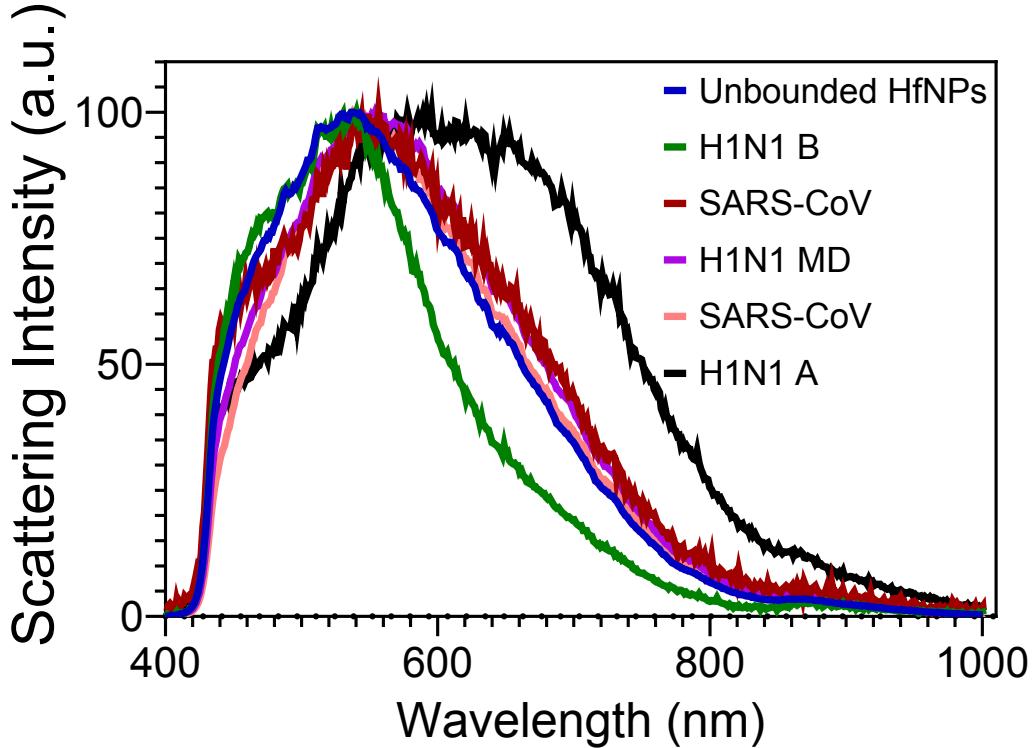
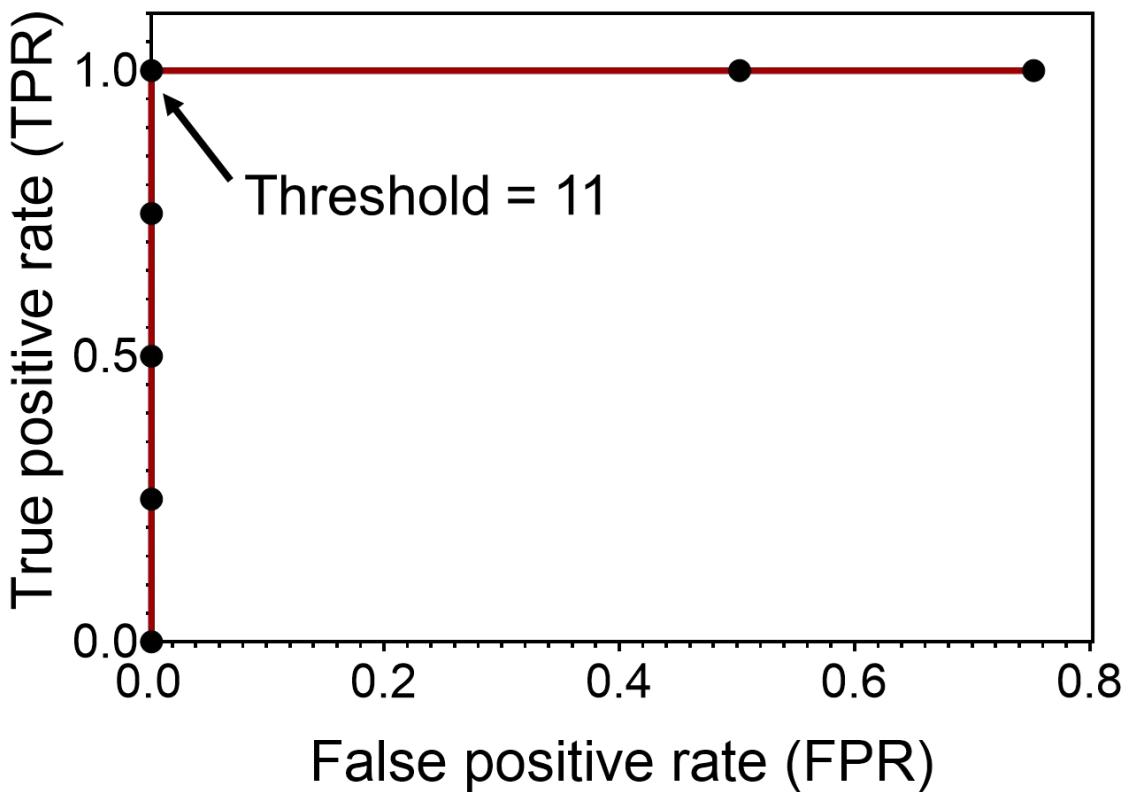


Fig. S12. Spectra collected using the hyperspectral technique for the unbound HfNPs functionalized with ASOs specific to the Influenza A H1N1 genetic materials in the presence of H1N1 A sample, SARS-CoV, H1N1 MD, H1N1 B, and SARS-CoV-2. The data shows a significant right shift in the reflectance hyperspectral signal in the presence of its target (H1N1 A), whereas no obvious shift in the spectra were observed in the case of the off-targets viruses including SARS-CoV, H1N1 MD, and SARS-CoV-2. However, H1N1 B spectrum showed a shift from the unbound one to left, which can be easily distinguishable from the H1N1 A as a target for these particles.



**Fig. S13.** Receiver operating characteristic (ROC) curve of the HyperSENSE test corresponding to the Fig. 8 of the main text.